IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

LONZA WALKERSVILLE, INC., et al.	*	
Plaintiffs,	*	
v.	*	Civil Action No. 8:20-cv-03099-PX
ADVA BIOTECHNOLOGY LTD.	*	
Defendant.	*	

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MEMORANDUM OPINION

This Opinion addresses the propriety of Plaintiffs' Emergency Motion for a Temporary Restraining Order ("TRO") or Preliminary Injunction against Defendant Adva Biotechnology Ltd. ("Adva") (ECF No. 51). For the following reasons, the Court GRANTS the motion and preliminarily enjoins Adva's importation, sale and use of the "Adva X3" as more particularly described in the Order accompanying this opinion.

I. Background

For seventeen years, Plaintiff Lonza Walkersville, Inc. and its affiliate Octane Biotech Inc. (hereafter "Lonza") have devoted serious resources to the research, development, and manufacturing of autologous[1] point-of-care cell-therapy technology. ECF No. 47 at 7–8. Although such cell therapy has been available for years in the treatment of cancer and other serious illnesses, it is traditionally very costly and of limited application. This is so because the cells used to manufacture the therapeutics must first be extracted from the patient, then exported to a separate centralized cell manufacturing facility for processing, and then returned to the hospital or care clinic to be administered to the patient. Leung Aff. ¶ 21, Dec. 22, 2021. This

[1] Autologous therapy "require[s] the cells that are used in the cell therapy to be derived from the patient's own tissue." The therapy is "frequently custom-made for the patient and cannot be mass produced." Leung Decl. ¶ 20, Dec. 22, 2021.

process is often expensive, cumbersome, and protracted, wasting time that desperately ill patients do not have. *Id.*

To address these logistical limitations, Lonza developed the "Cocoon Platform" ("Cocoon"). The Cocoon is a self-contained "bioreactor incorporating an all-in-one cell therapy manufacturing technology." ECF No. 47 at 7 (citing Ostrout Decl. ¶¶ 7–8, Dec. 22, 2021). The Cocoon, in short, allows the manufacture of cell therapeutics to occur locally in a hospital, other clinical site, or in a decentralized manufacturing facility so that the therapeutic may be generated much closer to where the patient receives treatment. Ostrout Decl. ¶¶ 10–11, Dec. 22, 2021.

To bring the Cocoon to fruition, Lonza has invested millions of dollars in research and development and has undertaken the arduous process of obtaining FDA approval for commercial medical use. Ostrout Decl. ¶ 9, Dec. 22, 2021. After seventeen years in the making, the Cocoon was used on the first patient in the United States in September 2020. Kornweiss Decl.¶ 3 Ex. 1, Dec. 22, 2021.

Lonza however is now at an "inflection point," where it may begin direct marketing and sales of the Cocoon to healthcare facilities. ECF No. 47 at 8. The market for such self-contained technology is both nascent and very small. Only three manufacturers, including Lonza and Adva, offer a similar point-of-care device. Ostrout Decl.¶ 16, Dec. 22, 2021. Further, because the commercial sales of this kind of technology is at its infancy, new customers are likely to remain loyal to their first choice for downstream replacement, upgrades, or modifications to their system of choice. Ostrout Decl. ¶ 14, Dec. 22, 2021.

Since 2002, Lonza has obtained seven separate Patents for the technology used in the Cocoon. *See* ECF No. 47 at 8; ECF No. 17-1 ¶ 2. Lonza avers that Adva has infringed on multiple claims related to all seven. ECF No. 17-1 ¶ 2. For purposes of this motion, Lonza

focuses only on a handful of claims related to U.S. Patent No. 10,844,338 entitled "Automated Tissue Engineering System" (the "338 Patent"). ECF No. 47 at 8–9. Lonza more particularly maintains that Adva's direct competitor to the Cocoon, the "Adva X3," (hereafter "Adva X3" or "X3") violates claims 1, 5, 8 and 9 of the '338 Patent. *Id.*

Adva is a private Israeli company that competes with Lonza in the field of portable cell therapy devices and related services. ECF No. 17-1 ¶¶ 41, 47. Although Adva maintains no physical presence in the United States, nor has it yet to sell any products here, ECF No. 19-3 ¶ 6, it indisputably seeks to capture its own market share for such point-of-care devices. In January 2020, Adva presented the X3 for demonstration and sale at a large and well-established trade show, "Phacilitate Leaders World Conference" in Miami, Florida. ECF No. 17-1 ¶ 53. At a like kind tradeshow held shortly after, Adva compared its "SP Single Use System" to the Cocoon. ECF No. 17-1 ¶¶ 71–75. Later that year, Adva Business Development Director, Ofra Toldeo, boasted that Adva hopes to market its technology "soon" in the United States. ECF No. 17-4 at 3; *see also* ECF No. 32 at 1 (Adva is "targeting . . . international markets" and has "quite a few interested clients in . . . the US.").

Lonza, in response, issued several cease-and-desist letters to Adva, expressly warning that Lonza considered the X3 to infringe directly on its patents. ECF No. 47 at 10; ECF No. 1-13. The parties failed to resolve their differences. ECF No. 17-1 ¶¶ 54–60. Lonza thereafter filed this infringement suit on October 23, 2020.

Most recently, Lonza learned that Adva intends to import and display the X3 at the upcoming trade show, "Phacilitate Advanced Therapies Week" scheduled to take place in Miami, Florida, on January 25–28, 2022. Promotional materials describe the conference as the "most immersive expo for cell and gene therapy," and "[h]ome to the largest marketplace for

tools and tech," which "brings the global advanced therapies community together for the most important week for doing business in advanced therapies." Kornweiss Decl., Ex. 2–3, Dec. 22, 2021. Adva is scheduled to sponsor a conference session entitled "Implementing New and Enabled Technologies into Existing Processes for Improved Commercial Outcomes," during which Dr. Ohad Karnieli, Adva's founder, will present specifically on the Adva X3. *Id.*, Ex. 5, Dec. 22, 2021. This expected importation of the X3, at a minimum, says Lonza, directly infringes on the '338 Patent. ECF No. 47 at 10. Accordingly, Lonza urges this Court to enjoin Adva from importing, using, selling, or offering for sale the X3 into the United States pending the outcome of this case. For the following reasons, Lonza has demonstrated that injunctive relief is warranted.

II. Analysis

The Court applies Federal Circuit law to patent infringement actions, including related motions for relief. *See Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1451 n.12 (Fed. Cir. 1988). Emergency injunctive relief remains an "extraordinary" remedy. *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1375 (Fed. Cir. 2009); *cf. Dewhurst v. Century Aluminum Co.*, 649 F.3d 287, 290 (4th Cir. 2011) (quoting *Winter v. Nat. Res. Defense Council*, 555 U.S. 7, 22 (2008)) (internal quotation marks omitted). The burden of establishing the propriety of a temporary restraining order rests with the movants who must demonstrate, by a preponderance of the evidence, four well-established factors: (1) a likelihood of success on the merits; (2) a likelihood of suffering irreparable harm in the absence of preliminary relief; (3) that the balance of equities tips in the party's favor; and (4) that issuing the injunction is in the public interest. *Winter*, 555 U.S. at 20; *Dewhurst*, 649 F.3d at 290.

The Court examines each preliminary injunction factor in turn.

A. Likelihood of Success on Merits

1. Infringement of the '338 Patent

The Court first turns to Lonza's likelihood of success as to the '338 Patent infringement cause of action. To prove infringement, Lonza must not only demonstrate likely success as to infringement of at least one claim of the '338 Patent, but also that Lonza is likely to withstand Adva's challenges to patent validity and enforceability. *Purdue Pharma L.P. v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1363 (Fed. Cir. 2001).

The infringement analysis entails two steps. The first is determining the meaning and scope of the patent claims at issue. In doing so, the Court must ascertain whether the patent "claims," identify "the subject matter for which the statutory right to exclude is secured by the grant of the patent." *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1476 (Fed. Cir. 1998). The proper construction of the patent claims is an issue of law "exclusively within the province of the court," *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996), and "a correct claim construction is almost always a prerequisite for imposition of a preliminary injunction." *Chamberlain Group, Inc. v. Lear Corp.*, 516 F.3d 1331, 1340 (Fed. Cir. 2008). Once the Court has ascertained the scope of the claim construction, it next must determine whether the accused device meets all elements of the claim. *Purdue Pharma*, 237 F.3d at 1364–65.

The '338 Patent includes 20 claims. ECF No. 17-2 at 1. Lonza maintains that the X3 principally infringes on Claim 1 of the '338 Patent and four other dependent claims. ECF No. 47 at 13–19. Adva concentrates its response solely on Claim 1. *See generally* ECF No. 59. Thus, the Court confines claim construction accordingly.

Claim 1 of the '338 Patent requires any covered device to be:

> [a] A cell culture engineering module, the module comprising;
>
> [b] at least one bioreactor;
>
> [c] a fluid containment system in fluid communication with the at least one bioreactor;
>
> [d] and one or more sensors configured to detect changing environmental conditions as a function of time with respect to the progression of a cell culture in the at least one bioreactor, the one or more sensors configured to generate signals to a microprocessor to automatically monitor and automatically alter the changing environmental conditions responsive to requirements of different stages of the cell culture until completion of the cell culture.

ECF No. 17-2 col. 32 l. 64–col. 33 l. 11.

Adva does not meaningfully dispute that the X3 includes the first three aspects of Claim 1. Hr'g Tr. 163:14–24, Jan. 12, 2022. This concession is well supported by the record. The Adva X3 indisputably includes a cell culture engineering module consisting of at least one bioreactor, a fluid containment system, and a microprocessor that automatically monitors and alters the changing environmental conditions related to "different stages of the cell culture until completion of the cell culture." Leung Decl. ¶¶ 31–36, Dec. 22, 2021.

Adva instead argues that the X3 does not infringe on the '338 Patent when the last aspect of the claim regarding "cell culture" and "completion of the cell culture" is limited only to what is known as "adherent cell culture" or culturing "aimed at proliferating cells on scaffolds/substrates for purposes of producing a tissue implant," ECF No. 59 at 12, 23; *see also* ECF No. 17-2 (Patent cover page describing the patent as for an "automated tissue engineering system"). Thus, Adva urges the Court to limit this aspect of the claim as follows:

Claim Language	**Adva's Proposed Construction**
automatically alter the changing environmental conditions ***until completion of the cell culture***	automatically alter the changing environmental conditions ***at different stages of the cell culture until cell seeding on a proliferation substrate has matured into a functional tissue for implantation***

ECF No. 59 at 20 (citing Selker Decl. ¶¶ 49–60).

If the Court agrees with Adva's construction, then the X3, which is designed to culture cells exclusively via "suspension," is not covered by Claim 1. ECF No. 17-2 col. 2, ll. 47–55; ECF No. 59 at 25 (citing Selker Decl. ¶¶ 44, 65–68). Otherwise, if the claim is construed to include both adherent and suspension cell culturing, then there is no real dispute that the X3 infringes on the '338 Patent, and Lonza is likely to succeed in demonstrating infringement.

The Court begins this analysis, as it must, with the plain language of the claim. *Resonate Inc. v. Alleton Websystems*, 338 F.3d 1360, 1364 (Fed. Cir. 2003). Claim terms are generally given their customary meaning as understood by a person of ordinary skill in the art ("POSA") at the time of the invention and when read in the context of the patent's intrinsic record. *Thorner v. Sony Comput. Entm't Am., LLC,* 669 F.3d 1362, 1365–67 (Fed. Cir. 2012). The intrinsic record consists of the claims, the specification, and the patent's prosecution history. *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 861 (Fed. Cir. 2004) (citing *Masco Corp. v. United States*, 303 F.3d 1316, 1324(Fed. Cir. 2002)). A court may also "consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 331 (2015). Upon identifying the plain meaning of the disputed term according to a POSA, a court should look to "the patent's written description and drawings to determine whether that meaning is inconsistent with the patentee's use of the term." *Resonate Inc.*, 338 F.3d at 1364; *see also Hill-Rom Servs. Inc. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014) ("Claim terms are generally given their plain and ordinary meanings to one of skill in the art when read in the context of the specification and prosecution history.")

Here, the Court must focus on the plain meaning of the term "cell culture" and by

extension, "completion of the cell culture." The definition of "cell culture" no doubt, is one steeped in the field of biomedical sciences. And this judge is decidedly not a scientist. Evidently recognizing this Court's limitations, each party offered its own expert not only to opine on the relevant POSA, but next to interpret the scope of the term "cell culture" as used in the claim.

Lonza's expert, Dr. James C. Leung, is eminently qualified in the scientific disciplines of biomanufacturing, bioengineering, and chemical engineering. Hr'g Tr. 9:13–12:16, Jan. 12, 2022. For 35 years, Dr. Leung has devoted himself to research, development, and manufacturing of recombinant proteins for use in human therapeutics. Leung Decl. ¶ 13, Dec. 22, 2021. He has worked consistently in the field of biotechnology and biochemical engineering with pharmaceutical companies and in academia. Hr'g Tr. 9:13–12:16, Jan. 12, 2022. Relevant here, the heartland of his robust experience lies in tissue engineering, cell culture, and cell fermentation. *Id.* Dr. Leung testified with ease and great familiarity as to the relevant technology inherent in the '338 Patent and the Adva X3. He also defined basic biochemical terms. He credibly explained that cell culturing can be divided broadly as "adherent" cell culturing where cells grow together and attached to one another usually on a scaffold or matrix, and "suspension" cell culturing, where cells grow in a liquid medium. Hr'g Tr. 23:12–25, Jan. 12, 2022. Dr. Leung further explained that "cell culturing" constitutes a basic building block of any "tissue engineering." Hr'g Tr. 16:11–16, Jan. 12, 2022.

Adva's expert, Dr. Mark Selker, hails from a different discipline. He holds no degrees in bioengineering or biochemistry, but rather occupies the field of electrical engineering. ECF No. 59-3. He was qualified as an expert in measurement and control systems related to bioreactors and bioprocesses. Hr'g Tr. 76:16–18, Jan. 12, 2022; *see* ECF No. 59-3. Notably at the inception

of the '338 Patent in 2002, Dr. Selker was working for a telecommunication company. Hr'g Tr. 146:11–14, Jan. 12, 2022. And during his testimony, he candidly admitted that he was "not the expert" in the cellular processes which depend on suspended cell versus adherent culturing on a "scaffold" or matrix. Hr'g Tr. 145:16–146:10, Jan. 12, 2022; *see also* Hr'g Tr. 164:23–165:25, Jan. 12, 2022. ("I am not the expert on tissue engineering" and so cannot opine on whether cartilage cells are required to grow on a matrix); Hr'g Tr. 170:9–13, Jan. 12, 2022 (conceding no knowledge as to whether stem cells require a scaffold for growth in culturing).

Predictably, each party urges the Court to define the POSA relevant to the '338 Patent terms as closely aligned with their respective experts. Dr. Leung opines that the proper POSA is trained and experienced as "a biomedical and/or biochemical engineer with a Masters' degree or higher in that field, or related field with at least fifteen years of experience working in the field of biomanufacturing, biochemical engineering, or biomedical engineering." Leung Decl. ¶ 30 n.3, Dec. 22, 2021. Dr. Selker, in contrast, views the proper POSA as having "at least three years of direct industry experience in the field of bioprocessing and the design/implementation of bioreactors" and that has a Masters' degree or higher in a field of science that "facilitates understanding of the basic workings of bioreactors, their controls, and understands the basic needs of cells to proliferate in a bioreactor." Selker Decl.¶ 38.

The Court must credit Lonza's position as to the proper POSA. Indeed, the only real dispute in this motion concerns the meaning of "cell culture" and relatedly, the "completion of the cell culture" of the same. Cell culturing is a basic process inherent in all tissue engineering which falls squarely within the disciplines of biomedical and biochemical engineering. Hr'g Tr. 17:16–19:4, Jan. 12, 2022; Leung Decl. ¶ 44, Jan. 7, 2022. Thus, a POSA would occupy the field as Dr. Leung describes. Leung Decl. ¶ 30 n.3. Dr. Selker, by contrast, failed to explain

sufficiently why the POSA for the term "cell culture" or culmination of the same must have a particular expertise in bioreactors to the exclusion of biochemistry or biochemical engineering.[2] This seems especially problematic when Dr. Selker himself admits that important aspects of cell culturing is beyond his ken. Thus, the Court agrees that a POSA in this instance is one with substantial experience in biomanufacturing, biomedical or biochemical engineering.

For similar reasons, the Court likewise credits Dr. Leung's opinion as to defining the term "cell culture" and "culmination" of the cell culturing process as used in the '338 Patent. Dr. Leung explains that a POSA at the inception of the invention would understand "cell culture" to include both "adherent" and "suspension" culturing. Leung Decl. ¶¶ 33–34, Jan. 7, 2022. Similarly, as to the term "cell culture completion," Dr. Leung instructs that "the end of any process is a 'completion,'" and "completion of a cell culture" is understood simply as "completion of a desired stage of a cell culture" and is not limited to any particular final product, and certainly not limited to the final product of "tissue" ready for "implant." Leung Decl. ¶¶ 35–38, Jan. 7, 2022. Thus, the Court agrees with Lonza that a POSA would understand the term "cell culture" to include both suspension and adherent cell culturing.

Adva, in response, argues that the Court must limit the definition only to adherent cell culturing when read in the context of the entire '338 Patent. A court may depart from the plain and ordinary meaning of a disputed term only "1) when a patentee sets out a definition and acts as his own lexicographer, or 2) when the patentee disavows the full scope of the claim term either in the specification or during prosecution." *Hill-Rom Servs. Inc.*, 755 F.3d at 1371

[2] Dr. Selker's testimony focused much on the '338 Patent drawings to identify the inclusion of a "scaffold" or "matrix." *E.g.,* Hr'g Tr. 56–59, Jan. 12, 2022. But he failed to convince this Court that the availability of this structural option precluded using the technology for suspension cell culturing. *See infra.* at pp. 11–15.

(quoting *Thorner*, 669 F.3d at 1365). Neither circumstance applies here, and Dr. Leung's opinion is well-supported "in the context of the specification and prosecution history." *Id.*

With regard to definition of terms, the '338 Patent does expressly not define "cell culture." Indeed, nowhere does the Patent language plainly limit the term to either "adherent" or "suspension" culturing. *See generally* ECF No. 17-2; Leung Decl ¶ 36, Jan. 7, 2022. The Court thus finds no reason to limit the plain meaning of "cell culturing" based on the patentee as its own lexicographer. *Hill-Rom Servs. Inc.*, 755 F.3d at 1371.

Nor can the Court conclude that the reading of the terms in context limit "cell culture" solely to adherent culturing. Disavowal requires that "the specification [or prosecution history] makes clear that the invention does *not* include a particular feature." *SciMed Life System, Inc. v. Advanced Cardiovascular Sys, Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001) (emphasis added). Usually, such disclaimer is made clear by the patent description using such phrases as the "'present invention requires' or 'the present invention is' or 'all embodiments of the present invention are. . .'" *Hill-Rom Servs. Inc.*, 755 F.3d at 1371. Mere descriptions in certain embodiments not otherwise attributed to the whole of the invention cannot be read to limit the claim. *Id. (*"While we read claims in view of the specification of which they are a part, we do not read limitations from the embodiments in the specification into the claims."). No such language disclaims suspension cell culture in the '338 Patent.

Adva urges the Court to limit the term "cell culture" to "adherent" culturing culminating in a tissue ready for implant when reading the challenged terms in context of the patent language. It stresses that the term "suspension cell" culturing appears nowhere in the patent description. ECF No. 59 at 28–29 (citing Selker Decl. ¶¶ 31–32, 72). Adva also presses that reference to "stages" in the culturing process can only be considered as interim steps to the end product of

culturing tissue on a scaffold or matrix to be ready for implant. ECF No. 59 at 20–23. Adva's argument can only be described as selective reading.

A fair reading of the patent language supports rather than undermines that "cell culture" includes both suspension and adherent cell culturing, the completion of which is not restricted to tissue grown on a matrix of scaffold. Starting with the Summary of Invention, Adva stresses only the portion which aids its argument: "The system of the present invention is designed such that primary or precursor cells can be isolated from a donor tissue for further propagation, differentiation and production of a tissue implant," ECF No. 17-2 col. 3 ll. 30–33, and that the invention "is an automated tissue engineering system, the system comprising a housing that supports at least one bioreactor that facilitates . . . the generation of tissue constructs from cell and tissue sources," *id.* col. 3 ll. 35–39; ECF No. 59 at 22. From this, Adva argues that the Court must limit the patent only to devices that create tissue implant. ECF No. 59 at 20–23.

But the remainder of this summary squarely undermines Adva's argument. It makes clear that the "fully automated, portable and multifunctional" invention is designed to perform "one or more" myriad culturing processes "individually, sequentially or in certain predetermined partial sequences as desired or required." ECF No. 17-2 col. 3 ll. 15–20. Time and again, the description also makes clear that the invention is designed for "facilitating physiological cellular functions *and/or* the generation of one or more tissue constructs from cell *and/or* tissue sources." *Id.* at 1 (Abstract) (emphasis added). Thus, any attempts to read the limitation of "adherent" cell culture or "completion" as specific to creation of a "tissue implant" runs counter to, and is not consistent with, the entirety of the invention description.

Next as to the embodiments, although the specification does describe using the invention to culture tissue on a scaffold for implant, ECF No. 17-2 col. 2 ll. 47–57, many alternative

embodiments forecast use of the invention for suspended cell culturing. *See* ECF No. 17-2 cols. 9–10 (discussing alternative "aspects" of the invention to include methods for cell proliferation, seeding, expansion, washing); col. 10. ll. 26–44 (describing method for cell enrichment involving "loading a cell suspension containing excessive cell suspension volume into chamber" and continuously circulating "cell suspension"); col. 11 ll. 41–47 (describing automated cell culture techniques involving "cell expansion" used in cell therapy); col. 11 ll. 48–52 (describing use in pharmacological research performed on cells or tissues). This reading is consistent with the purpose behind the stated invention: to combine in one system "all of the steps of biopsy tissue digestion to yield dissociated cells, subsequent cell seeding on a proliferation substrate, cell number expansion, controlled differentiation, tissue formation and production of a tissue implant within a single automated tissue engineering system." *Id.* col. 1 ll. 60–67; Leung Decl. ¶ 39, Jan. 7, 2022; *see also* ECF No. 17-2 col. 2. ll. 59–63.

The '338 Patent specification also describes a variety of cell culturing processes not limited to growing tissue on a scaffold or matrix. *See* ECF No 17-2 col. 2 l. 59–col. 3 l. 34; ECF No. 62 ¶¶ 23–27. The invention, for instance, may be used for "cell washing and cell collection"—a process designed to remove undesired chemicals from a cell by loading the cells into the bioreactor as a cell suspension without a scaffold or other matrix. ECF No. 17-2 col. 10 ll. 26–24; Leung Decl. ¶ 24, Jan. 7, 2022. The process is completed when the cells are "washed," and the washed cell suspension collected. Leung Decl. ¶ 24, Jan. 7, 2022. The invention may likewise be used for "cell enrichment," ECF No. 17-2 col. 10 ll. 36–44, which "feeds" cells in suspension. *Id.*; Leung Decl. ¶ 25, Jan. 7, 2022. The invention also permits automated cell digestion where cells are disaggregated and made suitable for cell proliferation

and cell expansion. ECF No. 17-2 col. 4 ll. 35–40; Leung Decl. ¶ 26, Jan. 7, 2022. Each involves, and thus encompasses, cells suspended in a liquid medium.

Last, the '338 Patent provides that the "tissue engineering system . . . may be preprogrammed to perform each of the noted steps individually, sequentially or in certain predetermined partial sequences as desired or required." ECF No. 17-2 col. 3 ll. 15–20; *see also id.* col. 4 ll. 35–56 (discussing various embodiments that "can be done alone or sequentially as desired"); col. 32 ll. 61–63 ("although the preferred embodiments of the invention have been described herein in detail, it will be understood by those skilled in the art that variations may be made" without departing from the spirit or scope of the invention). Contrary to Adva's insistence that the claim is limited only to technology that produces a final tissue "implant," the '338 Patent embraces a flexible system that can be programmed to complete one or more discrete cellular culturing functions. Hr'g Tr. 49:12–50:3, Jan. 12, 2022. Thus, the Court finds no basis to limit the terms "cell culture" and "completion of cell culture" only to adherent cell culturing that culminates in tissue ready for implant.

Adva, in response, presses that the purpose of the invention—that is the problem the invention was designed to address—disclaims application to "suspension" cell culturing. This is so, says Adva, because the prior art addressed by the patent was limited to tissue construction readied for implant. ECF No. 59 at 23. The Court disagrees. The patent makes clear that shortcomings of the prior art applied to both "cell culturing" and "tissue implants," and concerned human manipulation of the culturing process. ECF No. 17-2 col. 1 l. 29–col. 2 l. 39. Thus, the invention's true value add was the creation of a "user-friendly, automated system for *cell culture and tissue engineering,"* that could be used "in a variety of clinical and research settings for both human and veterinary applications." ECF No. 17-2 col. 2 ll. 42–45 (emphasis

added). The problem to be solved, in short, was full automation of the cell culturing process generally, not just for creating tissue ready for implant.

In sum, the Court ascribes the plain meaning of "cell culture" from the perspective of a POSA as one that incorporates both suspension and adherent cell culturing. The Court similarly construes "completion of cell culturing" to refer to the end of the different kinds of cell culturing processes for which the invention is designed to accomplish. This construction is amply supported by the text and descriptions of the invention within the '338 Patent. Accordingly, because the Court construes the claims as written to cover both adherent and suspended cell culturing, no real dispute exists that the '338 Patent covers the X3. Lonza has demonstrated likelihood of success on the merits of its infringement claim. The Court next turns to whether Lonza may withstand Adva's challenges to the Patent's validity.

2. Defenses to Patent Validity

Adva next contends that even if Claim 1 is constructed as Lonza urges, then the Patent is invalid for two reasons. First, that the '338 Patent fails the "written description" requirement and second that the patent it is anticipated by prior art. At the preliminary injunction stage, it is important to articulate the respective burdens of proof on claimed defenses. Unlike at trial where Adva bears the burden of proof, Lonza must demonstrate a likelihood of success that Adva "will not prove that the patent is invalid." *Purdue Pharma*, 237 F.3d at 1365. Stated otherwise, Lonza must demonstrate at this stage that Adva's defenses "lack[] substantial merit." *Id.*; *see Edge Systems, LLC v. Aguila*, 635 Fed. App'x 897, 902 (Fed. Cir. 2015) (quoting *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1050 (Fed. Cir. 2010)) ("[T]he preliminary injunction 'should not issue if an alleged infringer raises a substantial question regarding either infringement or validity, i.e., the alleged infringer asserts an infringement or invalidity defense that the patentee has not

shown lacks substantial merit.'"); *Helifix Ltd. v. Blok-Lok, Ltd*., 208 F.3d 1339, 1351 (Fed. Cir. 2000) ("If the alleged infringer raises a substantial question concerning validity, i.e., asserts an invalidity defense that the patentee cannot prove 'lacks substantial merit,' the preliminary injunction should not issue."). With the burden of proof clear, the Court addresses each contention separately.

a. Written Description Requirement

The crux of Adva's argument is that if Claim 1 is read as broadly as Lonza urges—to cover "suspension cell culture" performed by the X3—then the '338 Patent fails the "written description requirement" of 35 U.S.C. § 112. To be sure, a valid patent must include a "written description of the invention" that conveys "with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." *Nuvo Pharms. (Ireland) Designated Activity Co. v. Dr. Reddy's Labs. Inc*., 923 F.3d 1368, 1376–77 (Fed. Cir. 2019) (quoting *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1348 (Fed. Cir. 2011)). "The essence of the written description requirement is that a patent applicant, as part of the bargain with the public, must describe his or her invention so that the public will know what it is and that he or she has truly made the claimed invention." *Nuvo Pharms*., 923 F.3d at 1377. Adva maintains that because the patent description nowhere uses the precise term "suspension cell culture," and instead describes generating "tissue constructs" via cells "implanted on a substrate or scaffold," the inventor cannot have adequately described the invention to cover suspension cell culturing. ECF No. 59 at 28–29.

This argument amounts to a variation on Adva's claim construction theme. And for the same reasons already discussed, this argument fails. The patent description throughout describes a variety of processes which may or must be conducted via suspension cell culturing. *See* ECF

No. 17-2 col. 2 l. 59–col. 3 l. 34; Leung Decl. ¶¶ 23–30, Jan. 7, 2022. Thus, for the reasons previously articulated, the Court finds that Lonza has demonstrated this defense lacks substantial merit

Relatedly, Adva argues that the patent specification fails "to show that the inventors possessed the idea of a "cell culture engineering module," if that phrase is construed to refer to cover a module used for suspension cell cultures. ECF No. 59 at 29. Adva correctly notes that the term "module" appears 84 times in the specification of the '338 Patent, and every time refers to a "tissue engineering module." *Id.* Accordingly, if Lonza's infringement argument holds water, then it did not meet the written description requirement and thus Lonza will not succeed in demonstrating patent validity. *Id.*

But this argument is defeated by the entirety of the patent language and the relevant science. As Dr. Leung credibly explained, a POSA would understand the term "cell culture" to include both suspension and adherent cell culture, and more to the point, that "cell culture" is a fundamental aspect of "tissue engineering." Leung Decl. ¶ 44, Jan. 7, 2022; Hr'g Tr. 22:10–25, Jan. 12, 2022. It is of no matter that the '338 Patent refers to the invention as a "tissue engineering module" as this is understood by a POSA to include cell culture which itself encompasses both adherent and suspension processes. Leung Decl. ¶¶ 33, 46–47, Jan. 7, 2022; Hr'g Tr. 23:2–25, Jan. 12, 2022. The lack of written description defense is without substantial basis and is likely to fail.

b. Anticipated by Prior Art

Adva next contends that Lonza cannot defeat the defense of anticipation by prior art. ECF No. 59 at 30. For the patent to be valid, it must be "novel," meaning that the claimed aspects of the invention were not previously covered or "anticipated" by inventions that came

before it. *See* 35 U.S.C. § 102(a)–(b). Where all elements and limitations in the patent have been previously described in a "single prior art reference," the patent is deemed "anticipated" and thus invalid. *Hakim v. Cannon Avent Group, PLC*, 479 F.3d 1313, 1319 (Fed. Cir. 2007).

Adva argues that the '338 Patent had been anticipated in a 1992 study published by Yuan Shi, Dewey D. Y. Ryu, and Sun Ho Park (hereafter "*Shi* study" or "*Shi*") in which the authors describe having employed a bioreactor module to culture mammalian cells. Selker Decl., App'x. F; *see also* Selker Decl. ¶¶ 81–98. Adva maintains that because each component of the 1992 module is also covered in the '338 Patent, the patent is invalid. Lonza responds that the device in *Shi* did not employ automated regulation of the cellular environment over time and according to preprogrammed parameters. Leung Decl. ¶ 52 (citing *Shi* study at 264), Jan. 7, 2022. Rather the *Shi* study expressly intended to, and did, keep such environmental factors constant within certain preset ranges. *Id.* Thus, the parties' dispute narrowly concerns whether the automated feature in the '338 Patent is anticipated by the *Shi* study.

In support of its argument, Adva relies exclusively on Dr. Selker. Dr. Selker opined that the "microcontroller" in the prior art acted as the functional equivalent of the microprocessor described in the '338 Patent to perform the same automation contemplated in the Lonza invention. Selker Decl. ¶¶ 90–98 (schematic mapping controllers for oxygen, pH, temperature and agitation to '338 claim covering a "microprocessor" used to "automatically monitor and automatically alter the changing environmental conditions" responsive to stages of cell culturing); Hr'g Tr. 135:7–139:2, Jan. 12, 2022 (opining "[t[here is really functionally no difference" between a microprocessor and microcontroller). The Court cannot credit Dr. Selker's opinion in this regard. For one, Dr. Selker's assertion that the "microprocessor" in the

'338 and "microcontroller" in the *Shi* study were identical lacks sufficient support.[3] Nor did Dr. Selker ever squarely rebut that the overarching goal of the *Shi* study was "not really to control the cell culture" through fully automated technology. Hr'g Tr. 42:11–43:9, Jan. 12, 2022. Rather, it was to study oxygen transfer rates in cell culturing more broadly. Leung Decl. ¶¶ 52–53, Jan. 7, 2022. This point supports that the prior art does not teach fully automated cell culturing controlled by a computer microprocessor that regulates cell growth per preprogrammed user parameters. *Id.* Accordingly, this aspect of the '338 Patent had not been taught by *Shi*. Thus, Lonza has demonstrated that the defense of anticipation by prior art lacks substantial basis and is unlikely to defeat infringement.

Having found that Lonza is likely to succeed on the merits of its infringement claim, the Court turns to the remaining elements for injunctive relief.

B. Irreparable Harm

The Court considers next whether Plaintiffs have shown a likelihood of irreparable harm. To be successful, the movant must demonstrate that the harm requiring immediate action is "neither remote nor speculative, but actual and imminent." *Direx Israel, Ltd. v. Breakthrough Med. Group,* 952 F.2d 802, 812 (4th Cir. 1991) (quoting *Tucker Anthony Realty Corp. v. Schlesinger*, 888 F.2d 969, 975 (2d Cir. 1989)). "[T]he irreparable harm inquiry seeks to measure harms that no damages payment, however great, could address." *Celsis In Vitro, Inc. v.*

[3] Dr. Selker concedes that the microcontroller in *Shi* is not necessarily the equivalent of a microprocessor articulated in the '338 Patent. Hr'g. Tr. 139:16–140:12, Jan. 12, 2022. And while Dr. Selker characterizes the distinction as "split[ting] hairs," he struggled to answer Adva's specific query as to whether *Shi* would meet the microprocessor limitation in the '338 Patent. *Id.* at 140:6–12 ("Q: [w]ould Shi meet that limitation with regard to either a microprocessor or a micro whatever you call it?" A: "I can't answer that question . . . I don't know the nuance or exact splitting hairs definition of CPU, which means central processing unit."); *see also id.* at 185:11–191:1 (acknowledging the device in Shi employed a "strip chart recorder" to print out data regarding environmental conditions during cell culturing, used "before you had computers that had great graphical interfaces."). Considering Dr. Selker's testimony as a whole, the Court cannot credit that the "microcontroller" expressed in the prior art is functionally the same as the "microprocessor" used to employ a fully automated cell culturing technology in the '338 Patent.

CellzDirect, Inc., 664 F.3d 922, 930 (Fed. Cir. 2012). "Price erosion, loss of goodwill, damage to reputation, and loss of business opportunities are all valid grounds for finding irreparable harm." *Id.* (quoting *Abbott Labs v. Sandoz, Inc.*, 544 F.3d 1341, 1362 (Fed. Cir. 2008). A plaintiff "seeking preliminary relief [must] demonstrate that irreparable injury is likely in the absence of an injunction." *Winter*, 555 U.S. at 22.

Lonza has demonstrated that if Adva imports and markets the X3 in the United States, Lonza will likely suffer the lost "business opportunities, lost sales and market share, damaged reputation and goodwill, and losses from price erosion." ECF No. 47 at 20. As to the relevant market, the record clearly reflects that only three companies—including the two parties—offer a portable, self-contained automated device to conduct autologous cell therapies serving point-of-care facilities. *Id.* at 21; Ostrout Decl. ¶ 16, Dec. 22, 2021. Given the size and nature of the relevant market, it is easy to see why a sale of Adva X3 would quite likely be a lost sale for Lonza. Ostrout Decl. ¶ 23, Dec. 22, 2021. This market reality also extends beyond the device to all related services and products. Ostrout Decl. ¶¶ 14, 22, 24, Dec. 22, 2021. In this respect, the Adva X3 compromises both future sales and its carefully cultivated loyal customer base with "no effective way to accurately quantify" the harm. ECF No. 47 at 23.

Adva's only real response is to artificially recast the relevant market so to include large established corporations that occupy the biopharmaceutical field generally. But this is certainly not the correct market for the competing point-of-care devices. As Lonza aptly points out, the pharmaceutical industry, framed as broadly as Adva suggests, better describes the purchasers of the Cocoon and X3, not the manufacturers. ECF No. 61 at 11–12.

In sum, when considering that the market for these products is small, nascent, and on the precipice of capturing important and potentially long-lasting market share, Lonza has established

that the injunctive relief is necessary to avoid irreparable harm. *See Presidio Components, Inc. v. Am. Tech. Ceramics Corp.*, 702 F.3d 1351, 1363 (Fed. Cir. 2012) ("Direct competition in the same market is certainly one factor suggesting strongly the potential for irreparable harm"); *Automated Merch. Sys., Inc. v. Crane Co.*, No. 3:08-CV-97, 2008 WL 11383753, at *14 (N.D. W. Va. Dec. 2, 2008) (irreparable harm when plaintiff demonstrated "that it will suffer a loss of market opportunities as consumers are diverted from its products to defendant's products because [infringing sales] result in a continuing relationship with consumers and retailers due to the parts and maintenance required."). To do otherwise would allow Adva wide latitude in undercutting Lonza's market share, effectively forcing Lonza to "compete against its own patented invention." *Metalcraft of Mayville, Inc. v. The Toro Co.*, 848 F.3d 1358, 1369 (Fed. Cir. 2017). The Court cannot see how such harms could ever be properly captured through money damages only.

C. Balance of Equities and the Public Interest

Likewise, the balance of equities and the public interest tips in favor of granting relief. Under this factor, "[t]he district court must weigh the harm to the moving party if the injunction is not granted against the harm to the non-moving party if the injunction is granted." *Metalcraft*, 848 F.3d at 1369 (quoting *Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1457 (Fed. Cir. 1988)). "In considering whether the public interest favors the grant of an injunction, the district court should focus on whether a critical public interest would be injured by the grant of injunctive relief." *Id.* (quoting *Hybritech*, 849 F.2d at 1458).

One primary public interest is to preserve the sanctity of the patent system as the backbone of innovation. *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383 (Fed. Cir. 2006). Where a patentee demonstrates likely infringement on a valid patent, the Court must

consider that absent injunction, the infringer is free to usurp the market benefits that should be accorded to the patent holder. *See Celsis*, 664 F.3d at 932 (public maintains interest in avoidance of "taking market benefits away from the patentee and giving them to the accused infringer."). As such, this public interest tips decidedly in Lonza's favor.

Adva responds that the public interest must account for the need to provide "lifesaving technologies" to those desperately in need of relevant therapeutics. ECF No. 59 at 41. But this rhetorical sleight of hand does not align with the facts. Granting the requested injunction does not "deprive" the public of the relevant technology. As Lonza points out, two other companies are at the ready to fill the need. ECF No. 61 at 17. Nor has Adva demonstrated that if it does not import the X3, somehow the supply chain for automated point-of-care cell therapeutics will be hopelessly stunted. The Court finds that injunctive relief, narrowly crafted, would serve rather than undermine the relevant public interests.

As to equities of the parties, it is undisputed that Lonza has invested handsomely in seventeen years of research and development culminating in the Cocoon. It has also invested in protecting its invention through a series of patents beginning in 2002 and culminating in the '338 Patent. ECF No. 17-1 ¶ 2, 26; *see generally* ECF No. 62-1 (provisional patent priority date). Absent preliminary relief, Adva will undercut these patents plainly by importing and marketing the X3 at the upcoming tradeshow and beyond. Adva, for its part, has not entered the U.S. market at all. It has generated no U.S. sales and has no current business activities that would be disrupted. ECF No. 47 at 26. The injunction, therefore, maintains the status quo, and notably has no impact on Adva's aggressive marketing worldwide. *See* ECF No. 32 at 1, Ex. A ("We are targeting both the Israeli and international markets. We have quite a few interested clients in Europe, the US, and the Far East."); ECF No. 48-2 (promoting the X3 as fulfilling the need to

provide "immune cell therapy for cancer patients worldwide"). For these reasons, the harms to Lonza in denying injunctive relief outweigh those that may be visited on Adva.

III. Scope of Injunctive Relief

Lonza seeks preliminary injunctive relief to prohibit Adva from "making, using, selling, offering to sell and importing into the United States" the Adva X3 or any colorable variations thereof. The Court agrees that the requested relief is consistent with the protections afforded Lonza under the '338 Patent. *See* 35 U.S.C. § 271. Accordingly, the Court grants preliminary injunctive relief such that Adva is so restrained until the conclusion of the case on the merits.

In the interim, pursuant to Federal Rule of Civil Procedure 65(c), the Court must fix a bond to be paid by Lonza. The Court retains discretion in the amount to be posted, "and where the risk of harm is remote, a nominal bond may suffice." *Potomac Conf. Grp. of Seventh-Day Adventists v. Takoma Acad.*, No. DKC 13-cv-1128, 2014 WL 857947, at *22 (D. Md. Mar.4, 2014). Lonza urges the Court to impose a $5,000 bond. ECF No. 47 at 29. Adva provides no input, argument, or position on the bond to be set. Given the likelihood that Lonza will succeed on the merits of its claim, the amount appears suitable and will be set without prejudice so that either party will be free to request future modification. *Potomac Conf. Grp. of Seventh-Day Adventists,* 2014 WL 857947, at *22.

A separate Order follows.

1/21/2022
Date

/s/
Paula Xinis
United States District Judge